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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
MARSCHEL, A	
ART UNIT	**PAPER NUMBER**
1631	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/591,366	Baldya et al.
Examiner	**Art Unit**
Ardin Marschel	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Jul 30, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-48 is/are pending in the applica

4a) Of the above, claim(s) 23-48 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-22 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 1-48 are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No. 3 also 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The elected claims are only directed to arrays whereas the title encompasses arrays as well as the use thereof.

Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are

considered, a sufficient amount for a *prima facie* case are discussed below.

In claim 1 the limitation is present that requires that each untranslated target sequence has a defined chromosomal location. It is noted that the specification summarizes a number of factors for array preparation on pages 11-15 but therein lacks any enabling guidance as to what parameters must be satisfied in order to determine a "defined chromosomal location" for each probe target, much less for the probe sequence itself on this issue. A thorough review of the remainder of the specification also reveals a lack of discussion regarding how this is determined. It is noted that it is well known that no two human chromosomes are identical and that significant variability as well as repetitive sequences exist especially in non-coding regions. It is noted that untranslated sequences are in such non-coding regions. The specification also acknowledges on page 9, lines 12-30, that hybridization may be performed under a variety of stringencies as well as complementarities between probe and target sequences. It is also noted that each probe sequence is generally different which requires different hybridization conditions for the same stringency. Thus, the problem of probe design for such arrays wherein the probes are targeted to defined untranslated sequence in a chromosomal sample is extremely complex. Such complexity without a word of guidance

as to how to practice this chromosomal location requirement across what is normally a large array of probes supports a lack of enablement rejection based on undue experimentation by which to design probes as well as define hybridization conditions for such an array so as to achieve the desired chromosomal specificity across such an array. It is noted that even for probes defined by instant claim 18 that there is no chromosomal location definition set forth nor any array hybridization conditions set forth for the usage of such an array.

Claim 18 is noted to cite specific primer pairs but nowhere is there defined a chromosomal location for the target of the probes corresponding to these pairs. Thus, an additional lack of enablement for claim 18 is that the probes defined by these primer pairs are useless without defining some chromosomal location and/or possibly linkage to a genetic disease locus, for example. It is noted that Table 1 defines enzymes and/or proteins for each of these primer pairs but nowhere indicates what use these are to be put to. It is thus undue experimentation to define a use for these probes without some guidance as to what that is.

Claims 18-22 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 19, line 3, the target and probe polynucleotides are described as "bound" to form stable target-probe complexes. This causes claims 19-22 to be vague and indefinite in that hybridization is not cited therein. Do applicants wish to include covalent ligation type binding or chemical cross linking binding either without hybridization or is hybridization required for said binding? Clarification via clearer claim wording is requested.

Claim 18 is vague and indefinite as to what amplification is meant therein. Is the amplification meant to be directed to the preparation of probes prior to array synthesis in preparation to immobilize them? Or, alternatively, are the probes amplified after being on the array in order to form a complex network of probes for better immobilization of target polynucleotides? Clarification via clearer claim wording is requested.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103,

the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-7, 9-17, and 19-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Duggan et al.[Nat. Genetics 21(Suppl.):10(1999)] in view of Schena et al.[Science 270(5235):467(1995)], taken further in view of Wilcox et al.[NAR 19(8):1837(1991)].

Duggan et al. reviews the making and using of cDNA microarrays for the profiling of gene expression as summarized in the title and abstract. The microarrays are designed and prepared a summarized on pages 10 and 11 in the sections entitled "Principle of method" and "Fabrication" as formulating microarrays of a plurality of individually spotted ESTs and/or PCR products of size approximately 0.6 - 2.4 kb or approximately 600-2400 bases in length. This range is deemed to overlap with the about 50 to about 500 nucleotide lengths in instant claim 1. It is noted also that Schena et al. is cited as reference 3 as also exemplifying such arrays and expression profiling uses thereon in Duggan et al. on page 10, first column, third full paragraph. Thus, Duggan et al. array practice is clearly motivated by Duggan et al. In Schena et al. the preparation of arrays of this type is summarized on page 470, in the section

entitled "REFERENCES AND NOTES" in Note 5 as deriving the probes of the array from poly(A) primed synthesis thus including the 3'untranslated section of these cDNA probes. It is noted that the instant probes are not limited to being "only" targeted to the 3'untranslated section of target transcripts. The 3'-terminal cDNA portion of the probes of such arrays is also described in Duggan et al. on page 10, second column, first sentence of the second full paragraph. The usage of poly(A) primed clones for cDNA hybridization as STSs as clearly including the 3'-untranslated portion of cDNAs as probes is more fully described in Wilcox et al. on page 1842, first column, second full paragraph. Wilcox et al. is motivated in order to document the presence of the 3'-untranslated regions of cDNAs made via oligo(A) primed synthesis. Thus, the basic arrays of the instant invention are fully described in the above combination of references. Certain specific instant claim limitations are described in Duggan et al. as follows. Instant claim 9 is directed to covalent immobilization of probes on arrays which is described in Duggan et al. on page 11, second column, second full paragraph, via ultraviolet crosslinking. Instant claims 10-13 are directed to rigid or flexible arrays of various materials as also described in Duggan et al. on page 11, second column, first full paragraph. Instant claims 14-16 are directed to various control probe practice which is described in Duggan et al. on

page 13, first column, last four lines, through the second column, line 11.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the arrays of Duggan et al. as further detailed in Schena et al. with poly(A) primed probes which contain the 3'-untranslated region of transcripts as verified in Wilcox et al. thus resulting in the practice of the instant invention.

Claims 1-17 and 19-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Duggan et al.[Nat. Genetics 21(Suppl.):10(1999)] in view of Schena et al.[Science 270(5235):467(1995)], taken further in view of Wilcox et al.[NAR 19(8):1837(1991)], and taken further in view of Fodor et al.(P/N 5,510,270).

The basic invention for array hybridization has been summarized above as described in the combination of Duggan et al., Schena et al., and Wilcox et al. wherein the size of the regions on such arrays include generic wide varieties of size species as motivated for such arrays as set forth in Fodor et al. in column 15, lines 20-27. Fodor et al. is directed to the preparation and use of hybridization arrays as the noted combination of references and is cited herein to indicate that the probe regions on such arrays include the sizes as set forth in instant claim 8.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the arrays of Duggan et al. as further detailed in Schena et al. with poly(A) primed probes which contain the 3'-untranslated region of transcripts as verified in Wilcox et al. with array size regions documented for such arrays in Fodor et al. thus resulting in the practice of the instant invention.

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See the specification at page 12, last line, and elsewhere in the specification.

It is noted that footnotes are present in the instant specification on pages 12 and 13 which will cause confusion as to where these should be printed during the issuance process of any patent that may result from this application. Applicants are requested to remove these footnotes and incorporate them into the regular text as appropriate.

In the specification on pages 32-35 the top margin as filed was so small that hole punching to assemble the file has punched out some of the top printed material. Applicants are required to

supply replacement pages for these pages with a larger top margin to overcome this problem.

Correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

October 5, 2001

Ardin H. Marschel

ARDIN H. MARSCHEL
PRIMARY EXAMINER